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Editorial – Seminars in Dialysis

Obesity as a barrier to kidney transplantation: time to eliminate the body weight bias?

Helen MacLaughlin^{1,2}

Katrina L Campbell^{3,4}

1 Department of Nutrition and Dietetics, King's College Hospital, London UK,

2 Bond University Nutrition and Dietetics Research Group, Faculty of Health Sciences and Medicine, Bond University, Robina, Australia

3 Allied Health Services, Metro North Hospital and Health Services, Herston, QLD, Australia

4 Centre for Applied Health Economics, Menzies Health Institute, Griffith University, Brisbane, QLD, Australia

ABSTRACT

There is clear evidence that survival rates following transplantation far exceed those for remaining on dialysis, regardless of body size measured by body mass index (BMI). Studies over the past 15 years also suggest little to no difference in long-term outcomes, including graft survival and mortality, irrespective of BMI, in contrast to earlier evidence. However, weight bias still exists, as access to kidney transplantation remains inequitable in centres using arbitrary BMI limits. Clinicians faced with the decision regarding listing based on body size are not helped by conflicting recommendations in national and international guidelines. Therefore, in clinical practice, obesity, and recommendations for weight loss, remain a controversial issue when assessing suitability for kidney transplantation.

Obesity management interventions in end-stage kidney disease (ESKD), whether for weight loss for transplantation listing or for slowing kidney disease progression, are under-explored in trial settings. Bariatric surgery is the most successful treatment for obesity, but carries increased risk in the ESKD population, and the desired outcome of kidney transplant listing is not guaranteed. Centers that limit transplants to those meeting arbitrary levels of body mass, rather than adopting an individualised assessment approach, may be unfairly depriving many ESKD patients of the survival and quality of life benefits derived from kidney transplantation. However, robotic kidney transplantation surgery holds promise for reducing perioperative risks related to obesity, and may therefore represent an opportunity to remove listing criteria based on size.

Keywords: Transplant; obesity, chronic kidney disease; weight loss; dialysis

Introduction

The use of BMI as an assessment criterion for kidney transplantation is out of step with current practice, which favors a personalized medicine approach. BMI, originally derived as a measure predictive of population level mortality risk, is now widely used as a surrogate for obesity; issues with the appropriateness of this will not be considered here [1]. This paper explores this evidence regarding obesity as a risk factor for post-transplant outcomes, graft survival and mortality.

Clinical Practice Guidelines for transplant assessment generally recommend an individualised approach to determining suitability based on body weight, shape and size; however, they are plagued by moderate-to-low certainty evidence, which leads to inconsistencies in practice, often resulting in recommendations for weight loss prior to kidney transplant waitlisting.

The UK Renal Association (UK-RA) [2] and the Kidney Health Australia – Caring for Australasians with Renal Impairment (KHA-CARI) [3] both recommend that obesity by itself (defined as a BMI $\geq 30 \text{ kg/m}^2$) should not preclude listing for transplantation (UK-RA and CARI, GRADE 2B and 1B, respectively), and that assessment should be individualised and cardiovascular risk factors be considered (2B and 1C). Both also suggest that the positive outcomes of transplantation may be diminished in those with a BMI $> 40 \text{ kg/m}^2$ (2B and 1C).

The European Renal Best Practice guideline group (ERBP) state that the association between BMI and patient survival is uncertain, and refrained from making a guideline statement on kidney transplant listing based on obesity itself [4]. Instead, they took the approach of recommending weight loss for potential candidates with a BMI $> 30 \text{ kg/m}^2$ (ungraded), cautioning against pharmacological therapy and bariatric surgery due to the increased risks associated with these treatments.

Obesity and kidney transplant outcomes

Recent systematic reviews on kidney transplant outcomes demonstrate an increased risk of delayed graft function with obesity [5-8]; however, the data on mortality and graft survival are less clear [5-12]. The inconsistent conclusions appear to be related to methodological differences of inclusion criteria, date range and statistical analyses. In 2014, Nicoletto et

al reported that obesity did not impact upon death or graft loss in studies published since 2003 [6]. However, in studies published prior to 2003, obesity (BMI >30kg/m²) was associated with more death and graft loss than was seen in those having a normal BMI range [6]. Meta analyses conducted by Lafranca et al (2016) and Sood et al (2015) report an increased unadjusted risk ratio (RR) and fully adjusted hazard ratio (HR) respectively, for mortality, with BMI >30kg/m² [5, 7]. However, neither study split the analysis into “modern” and “older” transplantation eras, which may explain the difference in mortality risk between these studies and that conducted by Nicoletto et al.

The combined risk ratio reported by Lafranca et al suggested an association of obesity with an increased mortality risk (RR 1.52; 95% CI 1.14-2.03) [7]. In the same study, the meta analysis of studies using fully adjusted regression analysis (rather than an absolute risk ratio) demonstrated no association between obesity and mortality after kidney transplantation (HR 1.10; 95% CI 0.89-1.15). This finding concurred with that of Hill et al, who used a similar methodology (HR 1.24; 95%CI 0.9-1.7) [8]. All of these reviews have suggested that it is factors associated with obesity, rather than obesity per se, that explains the differences between studies that have adjusted for potential confounders and those which have not.

Similarly, conflicting results are reported for BMI and graft survival. Meta-analyses indicate a small reduction in the unadjusted risk of graft failure in lower compared to higher BMI recipients (RR 0.97; 95% CI 0.96-0.99) [7] and a small increased risk of graft loss with higher BMI (adjusted HR 1.06; 95% CI 1.01-1.12) [8]; yet in the seven studies using generalized linear modeling there was no difference in graft survival between low and high BMI (HR 1.00; 95% CI 0.96-1.04) [7]. Studies based on US transplant recipient databases all demonstrate an increased risk of, or shorter time to, graft failure with increasing BMI [9-11]. In those with a BMI > 50 kg/m², the risk of 30-day perioperative mortality, length of hospital stay, delay in graft function and 1, 3 and 5 year mortality were all significantly greater than in any other BMI group [13].

Conversely, using data extracted from the UK Renal Registry and the National Health Service Blood and Transplant (NHSBT) database for the UK transplant recipient population, fully adjusted hazard ratios for graft survival and patient survival did not differ across BMI bands in transplanted patients, up to BMI >40kg/m² [12]. It may be relevant that this study included participants transplanted from 2004 onwards. Furthermore, the authors suggest that the differences in their findings

when compared to other registry studies may be attributed to robust cardiovascular assessment of all potential transplant recipients in the UK.

Regardless of these contrasting (and, when present, relatively minor) findings for graft and patient survival after transplantation, there is clear evidence indicating that outcomes after transplantation are superior to those on dialysis, at any level of BMI [12, 14]. There was a significant survival benefit, in fully adjusted analyses, across all BMI categories for all types of transplant, compared to remaining on the waitlist, in both the UK [12] and US registry-based studies [14]. Survival at 1 and 5 years improved across BMI categories up to BMI $>40\text{kg/m}^2$, compared with remaining on dialysis, and there was no level of BMI at which this survival benefit was not evident [12]. One caveat appeared in the subgroup of black patients with BMI $\geq 40\text{ kg/m}^2$, with no survival advantage with transplantation over dialysis; however, this analysis is likely to be underpowered given the small sample size of this group [14].

Weight bias in transplantation and transplant listing

In patients with high BMI, listing for transplantation remains biased against this group despite clear evidence of a survival advantage over remaining on dialysis. In the US, the proportion of wait-listed patients receiving a transplant peaks at 69% when BMI is $<18.5\text{kg/m}^2$, then decreases steadily as BMI increases, down to a low of 45% when BMI is $\geq 40\text{ kg/m}^2$ [15]. Up to 30% of exclusions from transplant listing can be attributed to obesity [16]. Data from the French Renal and Epidemiology Information Network (REIN) indicate that, after adjustment for potential confounding variables, the likelihood of transplantation falls as BMI increases above 30 kg/m^2 . Patients with a BMI of $>31\text{kg/m}^2$ are more likely to remain on dialysis than receive a kidney transplant (HR <1) [17]. Beyond this, patients with a BMI $\geq 40\text{ kg/m}^2$ were half as likely to undergo transplantation than those with a BMI between $21\text{--}31\text{ kg/m}^2$ [17]. Furthermore, in those with a BMI $\geq 30\text{kg/m}^2$ each 1kg/m^2 decrease in BMI is associated with a 9-11% increase in the likelihood of transplantation.

Weight bias in kidney transplantation waitlisting likely exists due to the short-term complications such as higher rates of wound complications, longer hospital stay and delayed graft function. These factors have a direct impact on transplant centre costs and measures of quality and excellence; avoiding transplantation in high BMI patients may be practiced in an attempt to improve these measures [18]. Weight bias is also based on outcome data from “older” eras of transplantation, that likely differ from outcomes in during the “modern” era (the last 15 years)

of kidney transplantation. There appears to be consistency in the findings of studies using data from the early 2000s onwards, demonstrating no difference in patient or graft survival with obesity, compared to the normal BMI category as the reference standard [6, 12]. This equivalence of outcomes is largely supported by the systematic review of findings using multivariate analyses adjusted for likely confounding variables [7, 8].

Weight management options – from lifestyle to bariatric surgery

As BMI remains as a gatekeeper for transplant listing, weight loss interventions, including bariatric surgery, must be undertaken to improve the likelihood for kidney transplant listing for individuals. This is the case even though well-conducted, prospective studies of intentional weight loss on short and long term post transplant outcomes are lacking. Successful transplantation listing after bariatric surgery has been reported in several studies; many of these are small case series, with 55-100% of those undergoing bariatric surgery being listed for, or receiving a kidney transplant during follow up [19-24].

More modest weight loss has been recorded with lifestyle approaches including dietary intervention with or without exercise. Weight management approaches in the CKD population are most frequently assessed prior to dialysis and appear to promote weight loss in a range of 2-10%, sustained for up to 24 months [25-26]. In this weight loss range, several studies have demonstrated improved metabolic health [25-26]. However, this field is limited by small RCTs with high risk of bias, with limited focus on transplant listing as outcomes.

Although bariatric surgery may be able to help patients become listed for or receive kidney transplants, the risks involved from such surgery for people with kidney disease exceed those of the general population. Complications increase as kidney function declines, with almost a 10% increased absolute risk of complication post bariatric surgery in those with stage 5 CKD [27]. Risk of mortality post bariatric surgery is 11 times higher in those with ESKD compared to those without CKD, with the absolute rate increasing from 12 to 157 deaths per 1000 person years [28]. These risks, as well as potential benefits should be explained to, and understood by, individuals as part of decision-making process.

Use of specialised centres for bariatric surgery in ESKD may reduce operative complications and length of stay. Improvements occurred in the last 25 patients compared to the first 25 in a series of 100 patients with CKD undergoing bariatric surgery in a single centre, identifying a

learning curve for surgery in this specific patient population [29]. Risk minimisation protocols may also help to identify and reduce risk. The London Renal Obesity Network developed a joint surgical and nephrology protocol for patients with CKD undergoing bariatric surgery. They outline the steps to be taken for assessment, preparation and post operative monitoring, to improve clarity around management of renal specific issues including, but not limited to, robust cardiovascular risk assessment and fluid management [30].

Many individuals and some guideline groups advocate for assessment of a patient's suitability for kidney transplantation on an individualized basis considering metabolic fitness and surgical feasibility. However, unwarranted bias in wait listing continues to exist due to arbitrary BMI limits, and bariatric surgery often needs to be considered. However, before bariatric surgery is routinely recommended based on BMI alone to ESKD patients seeking kidney transplantation, robust evidence from prospective studies of improvements in patient focused outcomes and long-term safety is required [31].

Could robotic transplants address the issue?

Robotic surgery shows promise as a solution to the problem of body size impeding kidney transplantation. Several studies have demonstrated significantly fewer, and often no, site infections in obese, robotic transplant recipients [32-34]. Outcomes up to 5 years post robotic-assisted transplantation have also been studied. Median BMI in the robotic cases was significantly higher than on the open controls (BMI; 42.3 (31.1-64.3) vs 36.8 (30.0-51.1)), yet there was no difference in patient and graft survival or transplant rejection at 5 years between groups [33]. Similarly, using data from the UNOS registry in the US from patients with BMI >40 kg/m², with higher BMI in the robotic transplant group compared to open surgery, there was no difference in patient or graft survival, or kidney function at 3 years post transplant [34].

Is it time to limit body weight bias in kidney transplantation?

Bariatric surgery does lead to effective weight loss in patients with ESKD, but is not without risk and, of course, does not guarantee transplantation. Benefits may only outweigh the risks when the end goal of transplantation is achieved. In order to avoid potentially unwarranted weight loss surgery, referral to a specialist centre for robotic surgery should be considered in patients whose BMI is > 40kg/m²; this may help reduce the current trend towards bariatric surgery. With robust pre-transplant recipient assessment, sound medical management, risk assessment and modern era immunosuppression, weight loss prior to

transplantation is unlikely to further improve outcomes, and can increase the time on dialysis prior to transplantation. Certainly, when individualized assessment and cardiovascular disease risk assessment does not preclude transplantation, listing should occur without reference to BMI, provided all other listing assessment criteria are met.

This area is ripe for new research to address many of the conundrums faced. First, there is a need to continue to evaluate outcomes from robotic transplant procedures. Second, further evaluation of frailty and functional capacity, independent of body size, on transplant outcomes is needed. This may pave the way for clinical trials using nutrition and exercise interventions pre-transplant, with a focus on more patient-centered outcomes, rather than BMI, to optimise metabolic health prior to kidney transplantation.

References

1. Carrero JJ , Avesani CM. Pros and cons of body mass index as a nutritional and risk assessment tool in dialysis patients. *Semin Dial* 2015; 28: 48-58
2. Dudley C , Harden P. Renal Association Clinical Practice Guideline on the assessment of the potential kidney transplant recipient. *Nephron Clin Pract* 2011; 118 Suppl 1: c209-224
3. Russell C. *Obesity in renal transplantation*. The KHA-CARI Guidelines 2011 [cited 2019 26 January]; Available from: http://www.cari.org.au/Transplantation/transplantation_recipient_assessment/Obesity_in_renal_transplant.pdf.
4. ERBP Guideline on the Management and Evaluation of the Kidney Donor and Recipient. *Nephrol Dial Transplant* 2013; 28 Suppl 2: ii1-71
5. Sood A, Hakim DN , Hakim NS. Consequences of Recipient Obesity on Postoperative Outcomes in a Renal Transplant: A Systematic Review and Meta-Analysis. *Experimental and clinical transplantation : official journal of the Middle East Society for Organ Transplantation* 2016; 14: 121-128
6. Nicoletto BB, Fonseca NK, Manfro RC, Goncalves LF, Leitao CB , Souza GC. Effects of obesity on kidney transplantation outcomes: a systematic review and meta-analysis. *Transplantation* 2014; 98: 167-176
7. Lafranca JA, JN IJ, Betjes MG , Dor FJ. Body mass index and outcome in renal transplant recipients: a systematic review and meta-analysis. *BMC Med* 2015; 13: 111
8. Hill CJ, Courtney AE, Cardwell CR *et al*. Recipient obesity and outcomes after kidney transplantation: a systematic review and meta-analysis. *Nephrol Dial Transplant* 2015; 30: 1403-1411
9. Cannon RM, Jones CM, Hughes MG, Eng M , Marvin MR. The Impact of Recipient Obesity on Outcomes After Renal Transplantation. *Annals of Surgery* 2013; 257: 978-984
10. Kwan JM, Hajjiri Z, Metwally A, Finn PW , Perkins DL. Effect of the Obesity Epidemic on Kidney Transplantation: Obesity Is Independent of Diabetes as a Risk Factor for Adverse Renal Transplant Outcomes. *PLoS One* 2016; 11: e0165712
11. Naik AS, Sakhuja A, Cibrik DM, Ojo AO, Samaniego-Picota MD , Lentine KL. The Impact of Obesity on Allograft Failure After Kidney Transplantation: A Competing Risks Analysis. *Transplantation* 2016; 100: 1963-1969
12. Krishnan N, Higgins R, Short A *et al*. Kidney Transplantation Significantly Improves Patient and Graft Survival Irrespective of BMI: A Cohort Study. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* 2015; 15: 2378-2386
13. Kanthawar P, Mei X, Daily MF *et al*. Kidney Transplant Outcomes in the Super Obese: A National Study From the UNOS Dataset. *World J Surg* 2016; 40: 2808-2815
14. Gill JS, Lan J, Dong J *et al*. The survival benefit of kidney transplantation in obese patients. *Am J Transplant* 2013; 13: 2083-2090
15. Gill JS, Hendren E, Dong J, Johnston O , Gill J. Differential association of body mass index with access to kidney transplantation in men and women. *Clin J Am Soc Nephrol* 2014; 9: 951-959

16. Toapanta-Gaibor NG, Suner-Poblet M, Cintra-Cabrera M *et al.* Reasons for Noninclusion on the Kidney Transplant Waiting List: Analysis in a Set of Hemodialysis Centers. *Transplant Proc* 2018; 50: 553-554
17. Lassalle M, Fezeu LK, Couchoud C, Hannedouche T, Massy ZA , Czernichow S. Obesity and access to kidney transplantation in patients starting dialysis: A prospective cohort study. *PLoS One* 2017; 12: e0176616
18. Detwiler RK. Con: Weight loss prior to transplant: no. *Nephrol Dial Transplant* 2015; 30: 1805-1809
19. Kim Y, Jung AD, Dhar VK *et al.* Laparoscopic sleeve gastrectomy improves renal transplant candidacy and posttransplant outcomes in morbidly obese patients. *Am J Transplant* 2018; 18: 410-416
20. Al-Bahri S, Fakhry TK, Gonzalvo JP , Murr MM. Bariatric Surgery as a Bridge to Renal Transplantation in Patients with End-Stage Renal Disease. *Obes Surg* 2017; 27: 2951-2955
21. Kienzl-Wagner K, Weissenbacher A, Gehwolf P, Wykypiel H, Ofner D , Schneeberger S. Laparoscopic sleeve gastrectomy: gateway to kidney transplantation. *Surg Obes Relat Dis* 2017; 13: 909-915
22. Carandina S, Genser L, Bossi M *et al.* Laparoscopic Sleeve Gastrectomy in Kidney Transplant Candidates: a Case Series. *Obes Surg* 2017; 27: 2613-2618
23. Freeman CM, Woodle ES, Shi J *et al.* Addressing morbid obesity as a barrier to renal transplantation with laparoscopic sleeve gastrectomy. *Am J Transplant* 2015; 15: 1360-1368
24. MacLaughlin HL, Hall WL, Patel AG , Macdougall IC. Laparoscopic Sleeve Gastrectomy is a Novel and Effective Treatment for Obesity in Patients with Chronic Kidney Disease. *Obes Surg* 2012; 22: 119-123
25. MacLaughlin HL, Cook SA, Kariyawasam D, Roseke M, van Niekerk M , Macdougall IC. Nonrandomized Trial of Weight Loss With Orlistat, Nutrition Education, Diet, and Exercise in Obese Patients With CKD: 2-Year Follow-up. *American Journal of Kidney Diseases* 2010; 55: 69-76
26. Ikizler TA, Robinson-Cohen C, Ellis C *et al.* Metabolic Effects of Diet and Exercise in Patients with Moderate to Severe CKD: A Randomized Clinical Trial. *Journal of the American Society of Nephrology* 2018; 29: 250-259
27. Turgeon NA, Perez S, Mondestin M *et al.* The impact of renal function on outcomes of bariatric surgery. *Journal of the American Society of Nephrology* 2012; 23: 885-894
28. Cohen JB, Tewksbury CM, Torres Landa S, Williams NN , Dumon KR. National Postoperative Bariatric Surgery Outcomes in Patients with Chronic Kidney Disease and End-Stage Kidney Disease. *Obes Surg* 2018
29. Kim Y, Shi J, Freeman CM *et al.* Addressing the challenges of sleeve gastrectomy in end-stage renal disease: Analysis of 100 consecutive renal failure patients. *Surgery* 2017; 162: 358-365
30. MacLaughlin HL, Macdougall, I.C., Finer, N., Johansson, L., Frankel, A.H. The London Renal Obesity Network protocol for bariatric surgery in patients with chronic kidney disease. *British Journal of Renal Medicine* 2016; 21: 32-35
31. Chan G, Garneau P , Hajjar R. The impact and treatment of obesity in kidney transplant candidates and recipients. *Can J Kidney Health Dis* 2015; 2: 26
32. Oberholzer J, Giulianotti P, Danielson KK *et al.* Minimally invasive robotic kidney transplantation for obese patients previously denied access to transplantation. *Am J Transplant* 2013; 13: 721-728

33. Spaggiari M, Lendacki FR, Di Bella C *et al.* Minimally invasive, robot-assisted procedure for kidney transplantation among morbidly obese: Positive outcomes at 5 years post-transplant. *Clin Transplant* 2018; 32: e13404
34. Garcia-Roca R, Garcia-Aroz S, Tzvetanov I, Jeon H, Oberholzer J , Benedetti E. Single Center Experience With Robotic Kidney Transplantation for Recipients With BMI of 40 kg/m² Or Greater: A Comparison With the UNOS Registry. *Transplantation* 2017; 101: 191-196